

PATENT COOPERATION TREATY

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To:

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Broadgate House
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ROYAUME-UNI

Date of mailing (<i>day/month/year</i>) 04 January 2000 (04.01.00)	
Applicant's or agent's file reference REP06172WO	REPLY DUE see paragraph 1 below
International application No. PCT/GB99/03764	International filing date (<i>day/month/year</i>) 11 November 1999 (11.11.99)
Applicant CAMBRIDGE SENSORS LIMITED	

1. REPLY DUE within _____ months/days from the above date of mailing
 NO REPLY DUE, however, see below
 IMPORTANT COMMUNICATION
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2. COMMUNICATION:

Please be informed, in respect of the above-mentioned international application, that the receiving Office has informed the International Bureau that the International Filing Date should read :

11 November 1999 (11.11.99)

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08 November 1999 (08.11.99)

Copies: receiving Office (RO/GB)
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Designated States concerned.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer I. Britel Telephone No. (41-22) 338.83.38
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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

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NOTIFICATION OF ELECTION
(PCT Rule 61.2)Date of mailing (day/month/year)
18 July 2000 (18.07.00)

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
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in its capacity as elected Office

International application No.
PCT/GB99/03764Applicant's or agent's file reference
REP06172WOInternational filing date (day/month/year)
11 November 1999 (11.11.99)Priority date (day/month/year)
11 November 1998 (11.11.98)

Applicant

YON HIN, Bernadette et al

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

02 June 2000 (02.06.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12Q 1/00, G01N 35/00, 27/30, 27/327	A1	(11) International Publication Number: WO 00/28068 (43) International Publication Date: 18 May 2000 (18.05.00)
(21) International Application Number: PCT/GB99/03764		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
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(71) Applicant (<i>for all designated States except US</i>): CAMBRIDGE SENSORS LIMITED [GB/GB]; Downhams House, Downhams Lane, Cambridge CB4 1XT (GB).		
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(54) Title: ELECTRODE STRIPS FOR TESTING SMALL VOLUMES

(57) Abstract

A test strip comprising a support carries an active electrode and a counterelectrode, and a layer of material within which a small volume of liquid to be tested can be distributed and provide contact between the electrodes, and wherein an analyte-specific reagent is coated on the material. The layer of material can conveniently be provided in the form of a tape from which sections can be cut or used sequentially.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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Electrode Strips for Testing Small Volumes

Field of the Invention

This invention relates to electrode strips for testing small volumes of, say, whole blood.

5 Background of the Invention

Diabetes is one of the most common endocrine conditions. Sufferers must monitor their blood glucose level frequently. This is usually achieved by the use of small test strips which detect blood glucose.

Problems commonly experienced by users of these test strips are an 10 inadequate amount of blood on the test strip and bad placement of the blood on the test strip. A number of devices have addressed this problem by using sample chambers that fill by capillary action. The sample is retained in close proximity to the electrodes which facilitate the measurement of the specific analyte in the sample; see EP-A-0170375 and US-A-5141868.

15 Such known devices comprise electrodes deposited on a non-conducting substrate, coated with a reagent system specific for the analyte of interest and housed within a cavity whose dimensions are sufficiently small to allow introduction of a sample, e.g. 2.5-3 μL in volume, by capillary action. The extent to which these devices can be miniaturized is limited by both the 20 manufacturing tolerances and the signal-to-noise ratio achievable with their chemistry.

US-5820551 discloses a test strip comprising a support carrying a working electrode and a counter electrode, and an enzyme and a mediator that are coated on the active electrode. A drop of whole blood can provide a 25 conducting path between the electrodes, and the concentration of glucose in the blood can be determined. The active electrode is exposed to a whole blood sample without an intervening membrane or other whole blood filter.

WO-A-98/55856 (published after the priority date claimed for this Application) discloses an analyte-specific reagent coated on the conductive 30 layer, and a monofilament mesh laid over the reagent and the reference electrode. A sample application area is provided at one edge of the mesh.

Summary of the Invention

According to a first aspect of the present invention, a test strip comprises a support carrying an active electrode and a counterelectrode, and a layer of a material within which a small volume of liquid to be tested can be distributed and provide contact between the electrodes, and wherein an analyte-specific reagent such as one component of a redox reaction, e.g. an enzyme, co-factor or mediator, is coated on the material. In particular, the invention provides a test strip for blood glucose, in which the sample requirement is very small, and efficient reaction kinetics are achieved by the application of the reagents in a novel manner.

The reagent-coated material may itself be in tape form. According to a second aspect of the invention, a flexible tape is of a material within which liquid can be distributed and on which are coated discrete areas of at least one component of a redox reaction.

15 Description of the Invention

In accordance with this invention, any one or more of the components of a redox reaction, e.g. an enzyme such as glucose oxidase or glucose dehydrogenase, a co-factor and a mediator may be applied to a mesh or membrane which is placed over the device. For the purpose of illustration only, the invention may be described with reference to an enzyme-coated mesh. Whichever component or components are used, when the sample is added, they are solubilised quickly and form an efficient reaction medium that can provide contact between the separate electrodes of the test strip. In this manner, the reaction will proceed rapidly and without diffusion barriers. This reaction configuration is particularly indicated in cases where the sample volume is low, the sample is viscous (such as with whole blood) and a rapid reaction is required.

In a typical embodiment of the invention, the sensor test strip consists of two electrodes, one of which acts as a working electrode and another which acts as a counter, reference electrode. The end of the working electrode that is exposed to the sample has a mediator in intimate contact with it. The test strip effectively provides a reaction chamber defined by these two electrodes

and an additional sheet, overlying the electrodes, which has been pre-coated with the redox enzyme and any necessary co-factor for that enzyme. The reaction chamber may also comprise further sheets of material and/or wetting agents, e.g. a surfactant, or cell-lysing materials (which may be placed in any one of the overlying sheets). In this manner, the active enzyme is not coated onto the conductor which forms the working electrode but is provided in a separate layer above it which, in turn, effectively forms the solution phase of the reaction chamber. When combined with lateral flow, conditions are created that approach efficient mixing in a stirred reaction chamber.

10 In an example of the invention, a silver chloride/silver reference/counter electrode is located adjacent to a carbon electrode. Typically, for this purpose, a pair of printed carbon electrodes is printed on a non-conducting substrate, and then silver/silver chloride is printed on one of the carbon electrodes to function as the reference/counter electrode. A non-conducting ink is printed over the carbon electrodes and the substrate, in order to define a portion of each electrode as a contact pad for insertion into a meter and another portion on each electrode away from the contact pad as the sensing area where the sample is received.

20 A mediator for the enzyme cofactor NADH is then prepared and deposited onto the electrode from aqueous solution by pipetting. A further layer containing NAD is then deposited onto the working electrode.

25 A monofilament mesh material is coated with a surfactant and then with a solution containing glucose dehydrogenase via pipetting, ink jet-coating or dip-coating, and is placed over the two electrodes to form a reaction chamber. This reaction chamber may be defined further by additional printing, or by the use of a top layer to form an edge fill cavity. For example, a second non-conducting ink printed on top of the mesh material, and then a cover tape is applied on top of the mesh in such a way as to leave an extended area of the mesh exposed for sample application.

30 The device allows the application of a small volume of sample (typically 1 µL or less) to the mesh extension. This is followed by flooding of the device

sensing area with sample, bringing it into intimate contact with the measuring electrodes.

Devices having an edge fill are described in WO-A-98/55856. They can be simply adapted, in accordance with the present invention. In particular, 5 reference may be made to Fig. 1 in WO-A-98/55856; components of this invention are the support (1), electrodes (2/3), mesh material (6) and tape (7); in addition, reagent is provided on the mesh material. Such a device can work by application at its edge, to a sample. This is particularly valuable in cases where it is difficult to extract the sample. Other configurations will be evident 10 to one skilled in the art, including combinations of one or more of the cofactor, mediator or the enzyme coated onto the overlying mesh or membrane sheets. The choice of combination may depend on the reaction kinetics of the various compounds.

In another embodiment of the device, the enzyme or the mediator is 15 coated on the sheet, the co-factor and the other of the mediator or the enzyme are coated onto the working electrode directly, and the sheet is capable of filtering the whole blood such that the active electrode sees a sample which is effectively free of whole blood cells. In this case, the haematocrit dependency of the result is substantially reduced. In this manner, the cell-filtering function 20 of a selected membrane may be combined with the rapid kinetics of having the some or all of the active elements of the reaction (the enzyme, mediator and the co-factor) in the membrane, to produce a highly effective device.

In summary, according to the present invention, a device is constructed by depositing one or more of the reagents required for the quantitation of an 25 analyte as a single or multiple layers on a fine mesh material or membrane; the deposited areas are of dimensions small enough to wet with a very small sample volume. The mesh or membrane can be used in both colorimetric and electrochemical devices.

A characteristic of this invention is that a reagent is applied precisely 30 onto a target area on a woven material such as polyester or nylon or other porous membrane. In use, this provides rapid solubilisation of the reagents in the presence of the sample. The reagent or reagents can be applied in a

number of different methods that result in the deposition of a known volume at a precise location and in a well-defined foot-print. These include the use of dispensing equipment such as a piston pump, syringe pump or on-demand ink-jet printer.

- 5 In a further embodiment, a flexible tape containing one or more reagents may be laminated to another flexible tape on which is printed a series of electrodes. Instead of cutting out individual sensors, the laminate (comprising a row or series of sensors) may be used sequentially, e.g. on being dispensed from a suitable dispenser. For this purpose, whether or not as a laminate, a
10 tape of the invention may be provided as a roll, and stored in sealed cassettes which may also contain desiccant. In use, the cassette may be inserted into a automatic dispenser from which the tape is wound out automatically by an indexing mechanism to reveal sequentially the discrete sensors. The action of this instrument is therefore analogous to the action of a film in a camera. In this
15 embodiment, the tape may also contain a red blood cell-lysing reagent such as saponin, in order to reduce the effect of haematocrit and haemoglobin in a whole blood sample. The tape may be further protected from moisture by being covered with a peelable film (e.g. of aluminium) that is automatically peeled off when the tape is dispensed from the cassette. When the sample is applied to
20 the sensor, the amount of analyte of interest in the sample may be determined electrochemically. Such determination can be conducted by known methods.

The following Example illustrates the invention.

Example

- A conductive ink material is printed onto a non-conducting polyester
25 sheet material by a screen-printing process. The conductive ink material consists of a mixture of graphite and carbon particles and a polymer binder in an organic solvent. After deposition of the conductive ink, solvents are removed in a forced air oven. A silver/silver chloride reference/counter electrode is printed onto one of each pair of printed carbon electrodes followed
30 by a non-conducting ink layer to define the contact pads and the sensor area.

A mediator such as Meldola Blue, Nile Blue or other suitable dye and the enzyme co-factor nicotinamide adenine dinucleotide (NAD) are deposited onto

the carbon electrode. Alternatively, the NAD is applied separately over the mediator from an aqueous ink.

The enzyme glucose dehydrogenase is deposited as uniform spots on a monofilament polyester mesh tape. This is achieved as follows:

- 5 (a) in a contact mode, where a drop formed at a dispenser tip in close proximity to the mesh is allowed to be transferred to the mesh by touching off the drop onto the mesh surface; or
- 10 (b) in a non-contact mode, where a drop formed by an ink-jet print-head or other orifice above the mesh is dropped onto the mesh from a distance under conditions which do not cause it to penetrate the mesh.

Upon drying, the spots spread to cover an area defined partly by the characteristics of the mesh weave and partly by the application conditions. Typically the areas covered by a 500 nL drop is 1.3 x 1.2 mm. The mesh tape is allowed to dry at room temperature.

15 The enzyme-modified mesh tape is then laminated onto the modified sheet of devices and secured further by a non-conducting print. Finally, a cover tape is laminated on top of the mesh. The sheets of devices are disc cut into individual devices. In an alternative device format, the laminated sheets are wound and included in a cassette type unit, allowing a single device to be used by a wind-on mechanism similar to a camera film-winding system.

CLAIMS

1. A test strip comprising a support carrying an active electrode and a counterelectrode, and a layer of material within which a small volume of liquid to be tested can be distributed and provide contact between the electrodes, and
5 wherein an analyte-specific reagent is coated on the material.
2. A test strip according to claim 1, wherein the reagent is at least one component of a redox reaction, e.g. one or more of an enzyme, a mediator and/or co-factor for the enzyme.
3. A test strip according to claim 2, wherein the at least one component
10 comprises the enzyme.
4. A test strip according to claim 2 or claim 3, wherein the enzyme is glucose oxidase or glucose dehydrogenase.
5. A test strip according to any preceding claim, wherein the material is a monofilament mesh or membrane.
- 15 6. A flexible tape of a material within which liquid can be distributed and on which are coated discrete areas of at least one component of a redox reaction.
7. A flexible tape according to claim 6, wherein the material is a monofilament mesh or membrane.
8. A container containing a wound tape according to claim 6 or claim 7.
- 20 9. A container according to claim 8 also comprising automatic dispensing means.
10. A method for testing a liquid for the presence of an analyte, which comprises contacting the liquid with a test strip according to any of claims 1 to 5, and detecting the current.
- 25 11. A method according to claim 10, wherein the liquid is blood and the analyte is glucose.

12. A test strip according to claim 5, which includes a sample application area at one edge of the mesh or membrane.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 99/03764

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/00 G01N35/00 G01N27/30 G01N27/327

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 02487 A (BOEHRINGER MANNHEIM CORP) 23 January 1997 (1997-01-23) page 1, line 33 -page 8, line 28; figure 1; table 1	1-5, 10, 11
Y	—	7-9
X	US 5 169 600 A (ISHIZAKA HIDEO ET AL) 8 December 1992 (1992-12-08) column 8, line 15-34	1
Y	—	7-9
X	US 5 779 867 A (SHIEH PAUL) 14 July 1998 (1998-07-14) column 4, line 14-21; claims 1-4 abstract	1-5, 10, 11
	—	—/—



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
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- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the International search

11 February 2000

Date of mailing of the International search report

24/02/2000

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INTERNATIONAL SEARCH REPORT

Int. Jpnal Application No
PCT/GB 99/03764

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 798 031 A (CHARLTON STEVEN C ET AL) 25 August 1998 (1998-08-25) abstract column 5, line 22-25	1-5, 10, 11
A		6-8
Y	US 5 628 890 A (CARTER NIGEL F ET AL) 13 May 1997 (1997-05-13) column 3, line 41 -column 4, line 10 abstract	1-5, 10, 11
Y	EP 0 230 472 A (MATSUSHITA ELECTRIC IND CO LTD) 5 August 1987 (1987-08-05) page 7, line 14-25	1-5, 10, 11
X	EP 0 593 096 A (MEDISENSE INC) 20 April 1994 (1994-04-20) page 6, line 57 -page 7, line 3; figure 3	6-9
A	page 2, line 28-50	1
X	US 4 218 421 A (MACK JOHN C JR ET AL) 19 August 1980 (1980-08-19) column 2, line 43 -column 4, line 53	6-9
X	US 5 679 311 A (HARTTIG HERBERT ET AL) 21 October 1997 (1997-10-21) abstract; figure 2A	6-8
A, P	WO 99 13100 A (ABBOTT LAB) 18 March 1999 (1999-03-18) abstract; figure 1	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

ISA International Application No

PCT/GB 99/03764

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9702487	A 23-01-1997	US 5762770 A			09-06-1998
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EP 0593096	A 20-04-1994	AU 622196 B			02-04-1992
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		JP 2112752 A			25-04-1990
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US 4218421	A 19-08-1980	NONE			

INTERNATIONAL SEARCH REPORT

Information on patent family members

National Application No

PCT/GB 99/03764

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5679311 A	21-10-1997	DE	4326339 A	09-02-1995
		EP	0637749 A	08-02-1995
		JP	2610109 B	14-05-1997
		JP	7077528 A	20-03-1995
		US	5609823 A	11-03-1997
WO 9913100 A	18-03-1999	AU	9129798 A	29-03-1999

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference REP06172WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/03764	International filing date (day/month/year) 11/11/1999	Priority date (day/month/year) 11/11/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/00		
Applicant CAMBRIDGE SENSORS LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 02/06/2000	Date of completion of this report 01.02.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Favre, N Telephone No. +49 89 2399 7363



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03764

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*):
Description, pages:

1-6 as originally filed

Claims, No.:

1-11 as originally filed

12 as received on 18/10/2000 with letter of 17/10/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

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5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
- copy of the earlier application whose priority has been claimed.
 - translation of the earlier application whose priority has been claimed.
2. This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:
- restricted the claims.
 - paid additional fees.
 - paid additional fees under protest.
 - neither restricted nor paid additional fees.
2. This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- complied with.
 - not complied with for the following reasons:
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary

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International application No. PCT/GB99/03764

examination in establishing this report:

- all parts.
- the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 12
	No: Claims 1-11
Inventive step (IS)	Yes: Claims 12
	No: Claims 1-11
Industrial applicability (IA)	Yes: Claims 1-12
	No: Claims

2. Citations and explanations **see separate sheet**

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

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Re Item II

Priority

The priority document does not refer to flexible tapes of a material within which liquid can be distributed and on which discrete areas are coated with at least one component of a redox reaction and to container containing wound tape. Therefore, the claimed priority date is not valid for the subject-matter of present claims 6-9.

However, the document "WO-A-13 100" cited in the search report as an intermediate document does not disclose elements which could infer with the novelty or inventive step of said claims 6-9.

Re Item IV

Lack of unity of invention

The separate groups of invention are the following:

Group I

Claims 1-5, 10 and 11: These claims refer to test strips comprising two electrodes and a layer of material on which an analyte-specific reagent is coated.

Group II

Claims 6-9: These claims refer to flexible tapes of a material within which liquid can be distributed and on which discrete areas are coated with at least one component of a redox reaction.

Given the absence of electrodes, which are essential features of the test strips of claims 1-5, 10 and 11, in the flexible tapes of claims 6-9, the above groups are not considered to be so linked as to form a single general inventive concept (Rule 13.1 PCT).

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International application No. PCT/GB99/03764

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Independent claim 1 refers to a test strip comprising (1) two electrodes and (2) a layer of material within which the liquid to be tested can be distributed and (3) on which material an analyte-specific reagent is coated. Moreover, claim 1 requires (4) the layer of material to provide contact between the electrodes.
 - 1.1 These features can be found in the test strip described in document D1 (US-A-5 779 867). The therein described sensor comprises 2 electrodes and a layer of material (carrier strip) which is in simultaneous contact with both electrodes (column 3, lines 14-23). The carrier strip readily absorbs aqueous assay samples and contains an enzyme system and an oxidizable dye.
 - 1.2 The features required by independent claim 1 can also be found in the sensor described in document D2 (EP-A-230 472). This sensor comprises electrodes covered by a perforated body having an enzyme and an electron acceptor, on which element the liquid sample to be tested is dropped (page 7, line 14 - page 8, line 11).
 - 1.3 The sensor described in document D3 (US-A-5 798 031) also comprises all the features required by independent claim 1 (column 2, lines 25-39 and column 5, lines 59-67).
 - 1.4 Therefore, the subject-matter of independent claim 1 is not novel over the disclosures of D1-D3 and thus does not meet the requirements of Article 33(2) PCT.
 - 1.5 Dependent claims 2-5 do not meet the requirements of the PCT in respect of novelty (Article 33(2) PCT). Documents D1-D3 all refer to enzymes. Documents D1 (column 5, line 25) and D2 (page 7, line 24) explicitly mention glucose oxidase. Moreover, D1 refers to paper (column 5, line 31-35) and D2 to a nylon non-woven fabric (page 7, line 23) as material within which the liquid to be tested is

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distributed.

- 1.6 Claims 10 and 11 refer to methods of testing a liquid, e.g. blood, for the presence of an analyte, e.g. glucose, using the test strips described in claims 1-5. However, said test strips are not novel (see points 1.-1.5 above) and documents D1-D3 all refer to the testing of blood for the presence of glucose. Therefore, claims 10 and 11 are not novel in the sense of Article 33(2) PCT.

- 1.7 The test strip defined in claim 12 differs from the prior art in that it includes a sample application area at one edge of the mesh or membrane, and not on top as disclosed in D1-D3 where the sample is dropped onto the center of the sample application area.
Thus the technical problem to be solved is to provide a device for use in the electrochemical analysis which device allows for sample collection without the need of aiming at the application area.
None of the prior art documents at hand discloses or fairly suggests the solution defined in claim 12. Moreover, said solution is not obvious *per se*.
Hence, claim 12 is considered to be novel and inventive in the sense of Articles 33(2) and 33(3) PCT.

2. Independent claim 6 refers to a flexible tape of a material (1) within which liquid can be distributed and (2) on which discrete areas are coated with at least one component of a redox reaction.
 - 2.1 Document D4 (US-A-4 218 421) describes a container storing and dispensing chemical reagent medical test strips in the form of a continuous band of such strips fastened together by a webbing or tape (column 2, lines 43-57). Given that D4 refers to urine chemistry, some of the test strips will be coated with at least one component of a redox reaction.

 - 2.2 Therefore, the disclosure of D4 is novelty destroying for the subject matter of claims 6 and 7, which thus do not fulfill the requirements of Article 33(2) PCT.

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3. Claims 8 and 9 refers to containers containing the tape described in claims 6 and 7. However, the content of a container is not a technical feature of said container *per se* and no other relevant technical feature is disclosed in the application as filed. Therefore, any container , e.g. those described in D4 (figure 2) or in D5 (US-A-5 679 311; figure 2a), is considered to be novelty destroying in the sense of Article 33(2) PCT for the subject-matter of claims 8 and 9.

Re Item VIII

Certain observations on the international application

1. The description (e.g. page 1, line 23 and page 2, line 29) refers to "working electrode" whereas the expression "active electrode" is used in claim 1. This expression should be clarified to meet the requirement of Article 6 PCT.
2. The relative term "small" used in claim 1 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
3. Claim 6 is not supported by the description as required by Article 6 PCT, as its scope is broader than justified by the description. The reason therefore is that claim 6 attempts to define the subject-matter in terms of results to be achieved, i.e. distribution of liquid and coating of discrete areas, without defining the technical feature required to achieve the required results.
4. The expression "wound tape" includes "a plaster to be put on a wound" and is thus confusing (Article 6 PCT). Claim 8 should be amended in order to remove this ambiguity.

mH

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference REP06172WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 03764	International filing date (<i>day/month/year</i>) 11/11/1999	(Earliest) Priority Date (<i>day/month/year</i>) 11/11/1998
Applicant CAMBRIDGE SENSORS LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/00 G01N35/00 G01N27/30 G01N27/327

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 02487 A (BOEHRINGER MANNHEIM CORP) 23 January 1997 (1997-01-23) page 1, line 33 -page 8, line 28; figure 1; table 1	1-5, 10, 11
Y	---	7-9
X	US 5 169 600 A (ISHIZAKA HIDEO ET AL) 8 December 1992 (1992-12-08) column 8, line 15-34	1
Y	---	7-9
X	US 5 779 867 A (SHIEH PAUL) 14 July 1998 (1998-07-14) column 4, line 14-21; claims 1-4 abstract	1-5, 10, 11
	---	-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

11 February 2000

Date of mailing of the international search report

24/02/2000

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 798 031 A (CHARLTON STEVEN C ET AL) 25 August 1998 (1998-08-25) abstract column 5, line 22-25 ---	1-5,10, 11
A	column 5, line 22-25 ---	6-8
Y	US 5 628 890 A (CARTER NIGEL F ET AL) 13 May 1997 (1997-05-13) column 3, line 41 -column 4, line 10 abstract ---	1-5,10, 11
Y	EP 0 230 472 A (MATSUSHITA ELECTRIC IND CO LTD) 5 August 1987 (1987-08-05) page 7, line 14-25 ---	1-5,10, 11
X	EP 0 593 096 A (MEDISENSE INC) 20 April 1994 (1994-04-20) page 6, line 57 -page 7, line 3; figure 3 page 2, line 28-50 ---	6-9
A	page 2, line 28-50 ---	1
X	US 4 218 421 A (MACK JOHN C ET AL) 19 August 1980 (1980-08-19) column 2, line 43 -column 4, 53 ---	6-9
X	US 5 679 311 A (HARTTIG HERBE 21 October 1997 (1997-10-21) abstract; figure 2A ---	6-8
A,P	WO 99 13100 A (ABBOTT LAB) 18 March 1999 (1999-03-18) abstract; figure 1 -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/03764

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5679311	A 21-10-1997	DE	4326339 A	09-02-1995
		EP	0637749 A	08-02-1995
		JP	2610109 B	14-05-1997
		JP	7077528 A	20-03-1995
		US	5609823 A	11-03-1997
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WO 9913100	A 18-03-1999	AU	9129798 A	29-03-1999
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